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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,471	09/12/2003	Robert E. W. Hancock	UBC1180-2	7167

28213 7590 01/23/2009

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
01/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,471	HANCOCK ET AL.	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-98 and 101-130* is/are pending in the application.

4a) Of the above claim(s) *89-92, 94-98* is/are withdrawn from consideration.

5)☒ Claim(s) *117-130* is/are allowed.

6)☒ Claim(s) *93,101-105 and 108-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/9/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

As noted previously, the present application has been transferred from former Examiner Young to the present Examiner.

Applicant's present response, including Affidavit/Declaration, is acknowledged and has overcome the rejections under 35 USC 112 1st rejection (Enablement) as to 2 of the 3 methods, but not the 1st (stimulating innate immunity using SEQ ID NO: 7), thus the Enablement Rejection of these claims remains.

Election/Restrictions

As noted previously, Applicant's election with traverse of Group V, claim 93 and 99-110, as drawn to the elected peptide of SEQ ID NO: 7, in the reply filed on 1/9/07 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to search other peptide sequences of the invention, e.g. SEQ ID NOS: 5-6, 8-10, and 13-17, since a search of some of these sequences would necessarily "reveal" art relevant to the sequences. This is not found persuasive for the reasons of record (see e.g. a comparison of 14 mer SEQ ID NO: 6 and 13 mer elected SEQ ID NO: 7, wherein no more than 3mer core is found identical). Additionally, Applicant has not supported the previous statement of record, that any art "revealed" would necessarily render obvious any of the other peptides beyond that of elected SEQ ID NO: 7. "Revealing" potential art and searching an actual distinct peptide structure as to whether "real" art exists on that peptide are two different things. Thus, a search of these distinct peptides must turn on a peptide by peptide analysis, there being no substantial core structure therebetween.

Claims 89-92 and 94-98 are withdrawn as being drawn to non-elected subject matter. Claims 93 and 99-110 are examined on the merits as drawn to the elected peptide of SEQ ID NO: 7.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112 1st Enablement

(1st Method only: "Stimulating Innate Immunity" using SEQ ID NO: 7)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 93, 101-105, 108-116 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained for the reasons of record, as to the 1st Method of Using SEQ ID NO: 7: for "stimulating innate immunity". Applicant's arguments have been fully considered, but are not found persuasive. There simply is insufficient evidence that SEQ ID NO: 7 alone, "stimulates" the loosely defined concept of "innate immunity". Applicant's submission via Affidavit/Declaration of the efficacy data of SEQ ID NO: 7 against bacterial infection, does not rise to the level of the Office being able to yet confer "treatment" and equating to "stimulating innate immunity".

(NOTE: Since the combination of any antibody, which is known already known to stimulate innate immunity - of which art could have alternatively been cited to any reference "comprising" an antibody and "any filler, adjuvant" thereof, which SEQ ID NO: 7 would necessarily, presently fall under the realm of).

The rejection is repeated below for continuity of record:

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Namely, peptide SEQ ID NO: 7 has not been shown to stimulate innate immunity within the immune system (the claimed invention), alone and absent the antibiotic or granulocyte-macrophage colony stimulating factor (GM-CSF), respectively it is administered in combination with – the latter already being known to carry out their functions respectively.

> The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the use of peptide SEQ ID NO: 7 has not been shown to stimulate innate immunity.

The nature of the invention: The invention is drawn to the combination of antibiotics or granulocyte-macrophage colony stimulating factor (GM-CSF) with peptide SEQ ID NO: 7, to stimulate innate immunity.

The state of the prior art and the predictability or lack thereof in the art:

Khan et al. (2002/0064501) teach that "[b]y way of example and not wishing to bound to theory, we propose that one of the mechanisms of immunoregulating peptide to modulate the immune response during pregnancy is the following: some IR factors during pregnancy can ensure that if T cells are activated, there is a bias to a Th2 response" (para 126). Thus, the ability of peptide to actually stimulate innate immunity is deemed theoretical.

And as noted previously, there is no prior art of record showing that the artificial 13mer peptide SEQ ID NO: 7, can function to carry out 'stimulation of innate immunity'.

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). Specification para 177 describes that: "Experiments were carried out with peptide and sub-optimal Cefepime given 6 hours after the onset of systemic S. aureus infection (FIG. 1). The data in FIG. 1 is presented as the mean.+-.standard error of viable counts from blood taken from the mice 24 hrs after the onset of infection. The combination of sub optimal antibiotic (cefepime) dosing and SEQ ID NO: 7 resulted in improved therapeutic efficacy. The ability of the peptides to work in combination with sub-optimal concentrations of an antibiotic in a murine infection model is an important finding. It suggests the potential for extending the life of antibiotics in the clinic and reducing incidence of antibiotic resistance." There is no discussion of SEQ ID NO: 7 alone or its ability

to stimulate innate immunity. Only a conclusion that SEQ ID NO: 7 works in synergy with Cefepime to improve S. aureus infection. And further conclude that SEQ ID NO: 7 must somehow "stimulate innate immunity", the claimed invention. At the present time, the above is deemed inconclusive evidence that SEQ ID NO: 7 works in any other way than that of a carrier alongside the combination with an antibiotic or GM-CSF, to either treat infection on the first front or stimulate innate immunity on the latter (or render anti-flammatory or anti-sepsis properties alone as in the claims), which those compounds are known to do alone.

The breadth of the claims and the quantity of experimentation needed: The claims are drawn broadly to the use of a peptide of SEQ ID NO: 7 to "stimulate innate immunity". There were no tests found conducted alone to substantiate the enablement of SEQ ID NO: 7 to carry out these functions, relevant to an infection or otherwise. As Khan teaches, the ability of peptides to stimulate innate immunity is purely hypothetical or theoretical at this stage. Absent further evidence (e.g. to something the Examiner overlooked in the specification or via 132 Declaration) there is insufficient teachings in the specification or art sufficient to overcome the teachings of unpredictability in the art as to enablement; it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Allowable Subject Matter

Notwithstanding the outstanding rejection, narrowed to a rejection of a method for "stimulating innate immunity" using SEQ ID NO: 7, the methods of treating inflammation and sepsis, using a peptide of SEQ ID NO: 7, were not found to be reasonably taught or suggested by

the prior art of record. The reasons for allowance are found in the Affidavit/Declaration submitted 8/21/09, pages 4-5, under the Title:

Efficacy against Inflammation

Which provide the test data of efficacy of SEQ ID NO: & in treating inflammation in *in vivo* infection models (Fig's 6-8).

And as Applicant notes on page 8, under the Title:

Efficacy in Sepsis Models

"As an extension of the anti-inflammatory activity elicited by SEQ ID NO: 7 [ ], a reduction in sepsis is expected. This is demonstrated by the upregulation of CCL5 (RANTES; Fig. 10), a positive prognosticator of sepsis outcome in a clinical setting, and by the activity of the related peptide, SEQ ID NO: 6 in a sepsis model (Fig. 11)."

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Claims 117-130 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 1/19/2008

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654